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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
09/602,508	06/23/00	BONNER-WEIR	S	10276-029001

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EXAMINER	
AFREMOVA, V	
ART UNIT	**PAPER NUMBER**
1651	8

DATE MAILED: 10/22/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application No.	Applicant(s)	
	09/602,508	BONNER-WEIR ET AL.	
	Examiner	Art Unit	
	Vera Afremova	1651	

-- Th MAILING DATE of this communication app ars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *1-13,27 and 28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: Notice to comply

DETAILED ACTION

Claims 1-28 are pending.

Election/Restrictions

Applicants' election without traverse of the invention of Group II (claims 14-26) in Paper No. 7 filed 8/03/2001 is acknowledged. Claims 1-13 (Group I), claim 27 (Group II) and claim 28 (Group IV) have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions.

Claims 14-26 are under examination in the instant office action.

Specification

The disclosure is objected to because of the following informalities:

The nucleotide and/or amino acid sequence disclosure contained in this application (see specification page 36, lines 8-9, and see specification page 42, seq. id. No. 1-6) does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825. See attached Notice to Comply.

Claim Rejections - 35 USC § 112

Claims 14-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

While applicant may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947). The term "dedifferentiated pancreatic cells" in claim 1 is used by the claim to mean "a population of pancreatic cells or ductal cells substantially free from islets cells

and obtained after islet isolation" while the accepted meaning is "dedifferentiation or redifferentiation of pancreatic exocrine cells to a duct-like phenotype". (see reference by Kerr-Conte et al. [U] at page 1112, a the bottom of col. 2). Thus, it is uncertain as claimed what is a starting material in the claimed method. Is it a population of ductal cells? Or is it a treated (dedifferentiated) islet cell population?

Claim 1 is indefinite with regard to the phrase "component" because it is not particularly clear whether it is a component of the extracellular matrix material or whether the extracellular matrix is a component of the whole culture system.

Claim 15 is indefinite because it is unclear whether the dedifferentiated cells were cultured till 70% confluency before or after adding matrix.

Claims 17 and 18 are indefinite because they contain improper Markush groups.

Claim 20 is indefinite because it is uncertain as claimed and as intended whether a commercial Matrigel preparation is intended (see specification examples, for example page 40, line 6) or whether another preparation obtained from EHS tumor cell similar to Matrigel is intended. However, no reference to other than Matrigel preparation derived from EHS is seen in the specification (page 17, lines 20-24).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14 and 16-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Kerr-1996
Conte et al. [U] or Rawdon et al. [V].

The claims are directed to a method of obtaining pancreatic islets wherein the method comprises steps of adding an extracellular matrix to population of dedifferentiated pancreatic cells, culturing the cells and obtaining pancreatic islet cells. Some claims are further drawn to the use of extracellular matrix such as collagen or derived from EHS tumor cells. Some claims are further drawn characterization of cells such as expansion and lack of insulin for dedifferentiated cells and hormone expression for islet cells.

Kerr-Conte et al. [U] disclose a method of obtaining or regenerating pancreatic islets wherein the method comprises steps of adding an extracellular matrix or 3D gels (Matrigel, rat tail collagen, bovine type collage) to a population of dedifferentiated pancreatic cells (ductal cysts obtained from human pancreatic islet preparation) , culturing the cells and obtaining/regenerating pancreatic islet cells (abstract or page 113, last par.). The references further disclose characterization of cells (see Fig. 5, for example) such as expansion dedifferentiated cells (ductal structure which are lacking insulin) and positive hormone expression for regenerated islet cells. The cited reference is considered to anticipate the present invention as claimed.

Rawdon et al. [V] disclose a method of obtaining pancreatic islets producing insulin wherein the method comprises steps of adding an extracellular matrix or Matrigel to a population of dedifferentiated pancreatic cells or epithelial component of dorsal buds of chick embryo, culturing the cells and obtaining pancreatic islet cells producing insulin (see abstract). The cited reference is considered to anticipate the present invention as claimed.

Claims 14-17 and 22-26 are rejected under 35 U.S.C. 102(b) as being anticipated by US 4,439,521 [IDS-AC].

The claims are directed to a method of obtaining pancreatic islets wherein the method comprises steps of adding an extracellular matrix to population of dedifferentiated pancreatic cells, culturing the cells and obtaining pancreatic islet cells. Some claims are further drawn to culturing cells until 70% of confluency. Some claims are further drawn characterization of cells such as expansion and lack of insulin for dedifferentiated cells and hormone expression for islet cells.

US 4,439,521 disclose a method of obtaining or regenerating pancreatic islets wherein the method comprises steps of adding an extracellular matrix (plastic dish) to a population of dedifferentiated pancreatic cells or ductal tissue free from islets (col. 9, line 16), culturing the cells till 70 % of confluency or attachment of ductal cells (col. 9, line 23) are and obtaining/regenerating pancreatic islet cells (col. 9, lines 45-68). The disclosed ductal cells/pieces are inherently lacking insulin and the regenerated islet cells are inherently hormone positive due to their nature as identified by the reference. The cited reference discloses two alternative methods for obtaining/regenerating islets wherein the starting material is either pancreatic duct (see col. 9-10 or see also col. 4 from line 60 till col. 40) or the starting material comprises pancreatic islet which are cultured to obtain attached ductal cells which are further produce regenerated islets after removal of floating or suspended cells (col.4, lines 5-13).

The cited patent is considered to anticipate the present invention as claimed.

Claims 14, 16-19 and 21-26 are rejected under 35 U.S.C. 102(b) as being anticipated by US 4,935,000 [A].

The claims are directed to a method of obtaining pancreatic islets wherein the method comprises steps of adding an extracellular matrix component to a population of dedifferentiated pancreatic cells, culturing the cells and obtaining pancreatic islet cells. Some claims are further drawn to the use of collagen as extracellular matrix component.

US 4,935,000 [A] teaches a method of obtaining pancreatic islets wherein the method comprises steps of adding an extracellular matrix or collagen containing mesenchyme to a population of differentiated pancreatic cells or to a pure population of adult ductal epithelial cells (example 1), culturing the cells and obtaining pancreatic islet cells producing insulin (table 1).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 14-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kerr-Conte et al. [U], Rawdon et al. [V], US 4,439,521 [IDS-AC] and US 4,935,000 [A] taken with US 5,681,587 [IDS-AB], US 4,829,000 [B] and Bonner-Weir et al. IDS-AR].

The claims are directed to a method of obtaining pancreatic islets wherein the method comprises steps of adding an extracellular matrix to a population of dedifferentiated pancreatic cells, culturing the cells and obtaining pancreatic islet cells. Some claims are further drawn to the use of extracellular matrix such as collagen or matrix derived from EHS tumor cells. Some

claims are further drawn to culturing cells until 70% of confluency. Some claims are further drawn characterization of cells such as expansion and lack of insulin for dedifferentiated cells and hormone expression for islet cells.

The cited references Kerr-Conte et al. [U], Rawdon et al. [V], US 4,439,521 [IDS-AC] and US 4,935,000 [A] are relied upon as explained above for the disclosure of method of obtaining/regenerating islets from dedifferentiated pancreatic cells. Some of the cited references are lacking the disclosure of a particular extracellular matrix materials in a method for producing islets. Some references are lacking the disclosure related to culturing cells till 70% confluency. However, the cited references combined teach all limitations of the presently claimed method. Moreover, some of them are suggesting/teaching Matrigel as a superior material for raising insulin-producing cells [V] or for dedifferentiation of pancreatic cells [U]. The other cited reference suggests//teaches a higher frequency of cell neogenesis at confluency at least 60-70% in a method for producing islets [A].

The additional references are relied upon for the disclosure of various matrix materials for producing cells including pancreatic islets {US 5,681,587[IDS-AB], US 4,829,000 [B]}.

Bonner-Weir et al. IDS-AR] is relied upon for the general idea of a method for producing pancreatic islets cells encompassing proliferation and subsequent differentiation of ductal epithelium or its precursor population (page 63 at conclusion).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to modify the methods of the cited references with a reasonable expectation in success in producing hormone positive or insulin producing islet cells because the idea of islets regeneration or neogenesis of islets from ductal cells or dedifferentiated pancreatic

cells has been known in the prior art as demonstrated by the cited references. The use of particular matrix for cell attachment of development is considered to be within the knowledge available to regular practitioner particularly in view that matrigel (EHS preparation) is known and suggested as superior material for producing islets. Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary. The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 U.S.C. 103.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (703) 308-9351. The examiner can normally be reached on 9.30 am - 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (703) 308-4743. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Vera Afremova
AU 1651
October 17, 2001.

SANDRA E. SAUCIER
PRIMARY EXAMINER